## REMARKS

Claims 1 and 5-11 were presented for examination. Claim 11 has been canceled. Reconsideration of the rejections in view of the following remarks is respectfully requested.

Rejections under 35 U.S.C. § 112

Claims 8-10 were rejected under 35 U.S.C. § 112. These claims relate to methods of using an improved amination reagent, which is related to ones known in the art but has better safety and handling characteristics than those previously known. The invention thus resides in the design of an amination reagent that has improved safety and handling characteristics, while maintaining suitable reactivity to perform the amination reactions.

The Examiner rejected the claims under 35 U.S.C. § 112, alleging that the 'recipient compound' of the claim was unclear, and that the reaction conditions were not adequately described. The applicant previously provided an affidavit demonstrating that the skilled person would have understood the term 'recipient compound' in the claims to describe compounds known to undergo N-amination with known aminating reagents having similar structures to the improved aminating agents of the invention. Thus the precise structures of the recipient compounds are readily determined by the person of ordinary skill without ambiguity or experimentation, from knowledge generally available in the art. See *Falkner v. Inglis*, 79 USPQ2d 1001 (Fed. Cir. 2006), saying that the written description requirement does not require working examples, actual reduction to practice, or recitation of information that is well known in the literature. The applicant also provided a number of references showing similar amination reactions, which demonstrate that such transformations using related aminating agents were well known in the art before this application was filed. The references demonstrate that conditions for using such amination reagents were well known. In addition, the specification describes use of nitro-substituted phenoxyamines related to the improved amination reagents of the claims, as reported in a cited reference (Boyles, et al., Org. Proc. Res. Dev., vol. 6, 230-33 (2002)). Boyles describes amination of quinazolinones with related aminating agents, and provides details about the conditions used (See Table 1); it also discusses the decomposition hazards associated with such aminating reagents (see, e.g., Table 2). Thus N-

amination reactions were known with related aminating agents, but the present aminating agents differ in their structure and stability over those in the prior art, while functioning similarly for N-amination reactions.

The Examiner maintained the rejections after the affidavit was submitted, alleging:

> The affidavit does not delineate the variations of conditions, starting materials, operating parameters, etc. for amination to proceed. Also, the examples provided in the affidavit are exclusively to heterocyclic nitrogen-containing compounds. Further, all of the examples provided in the affidavit are drawn to electrophilic amination reactions. Finally, the instant disclosure exclusively disclosed operability for the method using the instant claimed compound to aminate an indole comound wherein n of the instant claimed compound was 0. The affidavit has not provided support for the deficiency of the specification in supporting such a broad scope as set forth in instant claims 8-10. The metes and bounds of the method of claims 8-10 cannot be established due to a lack of written description and the vague terminology used.

The applicant respectfully traverses this rejection.

The Examiner correctly pointed out that the examples provided are drawn to heterocyclic nitrogen-containing compounds, which are N-aminated under electrophilic conditions. Since claim 8 recites amination of "a nitrogen in a recipient compound", only N-amination reactions are within the scope of the claims. The aminating agents of the claim are recognized in the art as electrophilic amination reagents, so of course the examples are all related to electrophilic amination reactions. The examples may all relate to cyclic compounds, which would be heterocyclic because they contain N; however, it is unclear how these observations support a rejection of the claims, since none of them demonstrate that the references fail to support the full scope of the claims.

The Examiner alleges that the reaction conditions were not delineated in the affidavit, and that the examples illustrate only amination of indole with compounds wherein n in formula (1) is 0. However, the affidavit and the plethora of cited references demonstrate that suitable reaction conditions were known when the application was filed: the applicant need not include that which was well known in the art at the time. MPEP 2164.01 ("A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332

(Fed. Cir. 1991).") The absence of detailed experimental conditions, where the invention resides in the selection of an improved aminating reagent, is not relevant to the written description analysis, as most those details relate to enablement. MPEP 2163: "Information which is well known in the art need not be described in detail in the specification. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)." The Examiner has not indicated that the rejection is based on enablement, but some of the language of the rejection could be interpreted as relating to enablement. However, the affidavit would rebut an enablement rejection, since it demonstrates that, based on the knowledge in the art at the time, no undue or non-routine experimentation would have been required to practice the full scope of the claimed invention.

The applicant also points out that *no* actual reduction to practice or actual working example is required to support a patent claim, thus the scope of the examples is irrelevant to the written description question. MPEP 2138.05. And there is clear evidence of a reduction to practice here, as well as an affidavit to demonstrate that the claimed methods work. In addition, the recent Federal Circuit decision in *Falkner v. Inglis* further clarifies that meeting the written description requirement does not require either working examples or express repetition of information that is known in the art. 79 USPQ2d 1001 (Fed. Cir. 2006). *Falkner* relates to a DNA sequence that was known in the literature, but not disclosed in the specification either directly or via incorporation by reference. The court said requiring recitation of the known sequence "would serve no goal of the written description requirement. It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention." *Id.* Likewise here, recitation of the known conditions for N-amination with reagents of this class, would add nothing to the relevant knowledge in the art, because suitable conditions are known; nor would recitation of more examples disclose any new information, where the existing examples demonstrate possession of the invention, as evidenced by the affidavit indicating that based on the specification, one of ordinary skill would expect the invention to operate according to the claims.

The affidavit states that the aminating reagents of the application would have been expected to aminate recipient compounds; that includes the aminating agents of the claims wherein n is not 0. The Examiner pointed to the examples as though the claims should be limited merely because the examples are limited to compounds where n = 0. However, the claims should not be limited by the examples, absent reasoning to show why the operability of the invention as claimed would be questioned. A single example is thus more than sufficient to support a genus claim, since case law demonstrates that no examples are required. See, e.g., *In re Rasmussen*, 650 F.2d 1212, 1214, 211 USPQ 323, 326-27 (CCPA 1981) (disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim to "adheringly applying" because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered); and *Falkner v. Inglis* (no working examples are required). The Examiner has provided no reasoning to suggest that the claimed aminating agents would not operate as claimed, regardless of whether n is 0 or 1-3, and the affidavit provides evidence to show that a person of ordinary skill would have expected them to work as claimed.

In summary, Claims 8-10 are drawn to an improved method for an N-amination reaction using certain aminating reagents having improved safety over ones known in the art. The scope of the claimed invention was clear to a person of ordinary skill at the time the application was filed, based on the affidavit, and no undue experimentation would have been required to practice the full scope of the invention. Any details not expressly disclosed relate only to information available in the art, such as specific conditions for practicing the claimed invention. The affidavit and references show that one of ordinary skill would have known the scope of the invention and how to practice it based on the specification as filed. The rejection of claims 8-10 under 35 U.S.C. 112 should therefore be withdrawn.

Finally, the Examiner said, "the broad scope as set forth in the instant claims 8-10" is not supported by the affidavit and specification. However, Claim 10 is drawn to N-amination where the recipient compound comprises indole, using an aminating agent that is fully described by chemical structure. The Examiner recognized that the amination of an indole was supported by the examples, and the scope of the aminating agent in these claims is far from 'broad'. Accordingly, claim 10

describes the recipient compounds and aminating agents with sufficient specificity to satisfy the written description requirement, even without resort to the affidavit, and the rejection of claim 10 under 35 U.S.C. § 112 should be withdrawn.

Rejections under 35 U.S.C. § 103

In the first paragraph of this rejection, which is identified as an obviousness rejection, the Examiner argued that rejection of claims 1-7 over Van Assche (US 4,472,194) or Tessier (US 4,801,717), is proper because "a reference that anticipates claim 7 would also anticipate claims 1-6." However, the Examiner did not identify any Species in the reference that could anticipate these claims. The applicant understands these references are applied ONLY for an obviousness rejection: no anticipation rejections are at issue. Accordingly, the rejection is understood to be an obviousness rejection, and the standards for an obviousness rejection applicable to chemical inventions as set forth in MPEP 2144.08 are applicable.

These claims (1, 5-7) relate to a genus of novel compounds. MPEP 2144.08 makes it very clear that a prior art compound genus does not render obvious every species or subgenus it may encompass. The MPEP says, "The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.")." The obviousness analysis of a chemical invention requires the Examiner to consider whether one would have been motivated to select the species or subgenus from the reference in view of the express teachings of the reference, the size of the prior art genus, structural similarities and differences, etc. (MPEP 2144.08.II.A.4) The mere fact that a compound can be constructed from the genus described in a reference is not sufficient to establish a *prima facie* case for obviousness rejection.

According to the Examiner, the claims were rejected over Van Assche "or" Tessier, but the rejection appears to rely on a combination of the references. As is explained in detail below,

neither reference alone can support an obviousness rejection, and the combination of these references is clearly improper because Tessier expressly excludes from its genus certain structural features that are *required* by the claims.

The Examiner asserted that both references clearly guided one to 4-nitro-2-trifluoromethyl and 4-trifluoromethyl-2-nitro substituted phenyl hydroxylamines. However, Tessier in fact expressly guides one away from having 2-nitro, 4-nitro, and 4-trifluoromethyl phenyl groups. Furthermore, the Examiner has not shown why one of ordinary skill would have been motivated to modify those allegedly disclosed species to arrive at the invention as claimed, or that, in view of the exclusions from the Tessier genus, one would expect them to work.

The Examiner previously pointed to claim 7, saying the only difference between it and the prior art is the absence in the prior art of the additional $CF_3$ required in claim 7. In support of that assertion, the Examiner pointed to language in Tessier allegedly describing "the base compound substituted 'with at least' one trifluoromethyl." That, however, is a grossly misleading representation of what Tessier discloses. Tessier discloses a very broad genus, beginning with Ar-$ONH_2$ where Ar can be any of a wide range of aryl or heteroaryl groups. Ar can be phenyl, in theory, but Tessier expressly excludes phenyl, phenyl with nitro in the 2 or 4 position, and 2-nitro-4-trifluoromethyl phenyl. It cannot fairly be said from this that Tessier 'suggests' using the compounds that the Examiner relied upon as 'base compounds' for a starting point: there is no justification for selecting those starting points based on Tessier. According to Tessier, Ar can be substituted with an unspecified number of substituents; but the Examiner has not shown why one of ordinary skill would have, based on Tessier, selected the number required to arrive at the claimed invention. The substituents disclosed in Tessier may include $CF_3$ within a long list, but Tessier's substituents cover a very wide array of structures. The Examiner has offered no valid justification for selecting the particular ones required to arrive at the claimed invention, or motivation for the particular placement of those substituents, in view of the express exclusions of, for example, 2-nitrophenyl, 4-trifluoromethylphenyl, and 4-nitrophenyl from the genus in Tessier..

Contrary to the examiner's assertion, it is not at all clear that the 'base compound' to which the Examiner refers is among the Ar groups that Tessier uses, because Tessier expressly excludes certain relevant species. Col. 2, lines 17-24. Tessier describes a genus that encompasses a *Huge* number of possible compounds, and teaches away from structural features that are essential to the claimed genus; yet the Examiner pointed to NO disclosure in Tessier that would guide someone toward the compounds alleged to be obvious. The Examiner has clearly not established a *prima facie* case for obviousness based on Tessier, and that rejection should be withdrawn.

With respect to Van Assche, the Examiner alleged that it discloses 'the base compound' of the claims, but has not identified motivation to modify that 'base compound' to provide a compound within the scope of the claims. Van Assche depicts a phenoxyamine that appears to have three substituents (see col. 1), but the identity and position of the substituents are actually precisely defined. It describes no 'optional' substituents in reality, only a number of very specific substitution patterns. It discloses in column 1 only one compound having a $CF_3$ group and a nitro group (there appear to be two, but both are actually the same 2-nitro-4-trifluoromethyl compound—one is called 6-nitro-4-trifluoromethyl, but that name describes the same compound); and only one compound with three substituents, which happens to have three nitro groups, putting it outside the scope of the present claims. It thus provides a precise description of a number of compounds, which are alleged to have biological activity. In view of its very narrow disclosure, the person of ordinary skill would not be motivated to modify its compounds to reach the claimed invention: there is no evidence in the reference to suggest that the biological activity would remain, or that modifications to the structure can be made, and certainly no guidance suggesting the modifications that would be required to arrive at the claimed invention. Van Assche does not disclose any compounds within the present claims, nor does it provide motivation to modify its disclosed compounds to reach the claimed genus. No *prima facie* case for such rejection based on Van Assche was established in the previous office action, and nothing was added in the latest office action to support an obviousness claim based on Van Assche. Therefore, this rejection should be withdrawn.

The Examiner stated in this rejection and the previous one that the claims were rejected over Van Assche "or" Tessier, but in the previous rejection, the Examiner appeared to combine the

disclosures of Tessier and Van Assche. The Examiner justified this by saying, "It is prima facie obvious to modify one known compound with *attributes* proven in analogous compounds." First, it is not clear at all what the Examiner's statement means, since 'analogous' is a vague term, and 'attributes' is such a general term. There must be some reason to 'modify' a compound and a reasonable expectation of success; as discussed below the relevant facts must be considered. The Federal Circuit has stated that "there are no *per se* rules of obviousness" (MPEP 2144.08: "Use of *per se* rules by Office personnel is improper for determining whether claimed subject matter would have been obvious under 35 U.S.C. 103. See, e.g., *In re Brouwer*, 77 F.3d 422, 425, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996); *In re Ochiai*, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995); *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994)"). The per se rule used by the Examiner, ("It is prima facie obvious to modify one known compound with *attributes* proven in analogous compounds.") is improper: the obviousness determination must be made in view of the facts of the situation. And here, in view of the express teaching away in Tessier from certain of the relevant substituent selections and placements, the person of ordinary skill would not have motivation tocombine the teachings as the Examiner has done, or a reasonable expectation of success when doing so.

Also, there is no proper justification for using Tessier to guide modification of the 'base compounds' allegedly disclosed in Van Assche: Tessier expressly excludes certain structural features that must be used to construct compounds of the present claims. Tessier excludes from its Ar groups phenyl, 2-nitrophenyl, 4-nitrophenyl, $CF_3$ in the 4-position, and 2-nitro-4-trifluoromethyl phenyl. In view of those exclusions one of ordinary skill would NOT be motivated to combine the teachings of the two references, because Tessier expressly teaches away from the very types of structures that are presently claimed, having nitro or $CF_3$ at positions 2 and 4, and having an additional substituent selected from a limited list (claim 1) or having, according to claim 7, an additional $CF_3$. Even if a *prima facie* case could otherwise be established, this exclusion by Tessier of highly relevant structural features is evidence to rebut it.

Therefore, no *prima facie* case for an obviousness rejection has been established based on either of the cited references, and the combination of references cannot properly be made. A

claimed subgenus cannot be rejected merely because it falls within a disclosed genus; and here, in view of the relevant exclusions from the genus in Tessier, the Examiner has not even established that the claimed genus is encompassed by one in the prior art. The obviousness rejection is thus overcome, and should be withdrawn.

The Examiner asserted that the instant specification provides examples only using certain compounds, and that "One must apply the same standard to the instant invention as has been applied to the prior art. If the prior art lacks guidance and motivation to make the compounds of the instant genus wherein the phenylhydroxylamine is trisubstituted, then the instant application would also lack guidance and motivation to make the compounds of the instant genus wherein the phenylhydroxylamine is trisubstituted. If however, the instant disclosure if [sic] supportive of the trisubstituted phenylhydroxylamines, then the prior art also supports such genus."

First, this is very confusing: the 'same standards' are clearly NOT applied to the claims under examination and to a cited reference. Indeed, the determination of obviousness MUST be done without reference to the applicant's disclosure. MPEP 2142. The Examiner has the burden to show that the reference meets the standards for an obviousness analysis with respect to the claims; otherwise, the claims are not rendered obvious by the reference. What the instant specification says is irrelevant to the obviousness analysis, unless it must be consulted for interpretation of the claims. The Examiner's statement is not consistent with the obviousness analysis, and it does not support a finding of obviousness.

New Rejection under 35 USC § 112

The Examiner has added a new rejection of claims 1 and 5-7, based on 35 U.S.C. § 112, alleging that "no description of the instant claimed compound of formula (1) wherein n = 1-3 could be found", and alleging that "The amendment of claims of n=1-3 represents NEW MATTER." The applicant traverses this rejection.

First, the rejection is clearly inapplicable to claim 5, which is limited to n = 1.

Second, a claim amendment is not 'new matter' merely because it is not taken verbatim from the specification. The Federal Circuit, in *In re Kaslow*, said, "The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language. *In re Edwards*, 558 F.2d 1349, 196 USPQ 465 (CCPA 1978); *In re Herschler*, 591 F.2d 693, 200 USPQ 711 (CCPA 1979). 217 USPQ 1089 (Fed. Cir. 1983). Thus the proper inquiry is the scope of the claim, not the particular way it is expressed. The amendment in question simply narrowed the claim from its original scope; thus the original claims and the description demonstrate possession of the claimed invention.

The inventor originally described a broader version of the invention claimed by the amended claim 1; the amendment excludes part of the original claim scope. As the Federal Circuit language quoted above indicates, verbatim support is not required for a claim limitation to be supported by the specification. Likewise, see MPEP 2163: "*Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* [i.e., "in the same words"] to be sufficient")." Here, the scope of the amended claim was inherently included entirely within the scope of original claim 1. In addition, original claim 5 named compounds having n = 1 as a preferred subgenus. Thus the applicant expressly disclosed both endpoints of the range n = 1-3 in the specification as filed, and one endpoint of that range (n = 1) is all that was amended. Since the added endpoint was expressly disclosed, the limitation of n = 1 is not new matter.

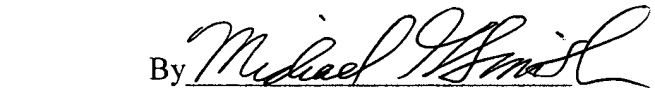
Here, claim 1 was amended to incorporate a new endpoint for a range of values for n; that endpoint was inherently within the scope of the original claims, thus the amended claims do not encompass any new subject matter; and the new endpoint, n = 1, was expressly disclosed as a claim limitation in the original application. Accordingly, the amendment does not add new matter, and this rejection should be withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. **219002030100**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: November 21, 2006

Respectfully submitted,

By 

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